IN THE DRAWINGS:

Please amend FIGS. 1-11B, as indicated in the replacement sheets of drawings below, to include the "Replacement Sheets" label in the top margin in compliance with 37 CFR 1.121(d). No new matter is introduced.

REMARKS

The present application was filed on July 10, 2003 with claims 1 through 21. Claims 6 and 16 have been previously canceled without prejudice. Claims 10-13 have been withdrawn from consideration in response to a restriction requirement, and herein Applicant proposes to cancel claims 2, 10-13 and 18 herein. Therefore, claims 1, 3-5, 7-9, 14, 15, 17 and 19-21 are presently pending in the above-identified patent application. Applicant herein proposes to amend claims 1, 14 and 21. Support for the amendments can be found, for example, on page 11, line 5 through page 12, line 20, and page 8, line 1 through page 9, line 5. No new matter is being introduced.

Additionally, Applicant proposes to amend all drawings (i.e. FIG. 1 through FIG. 11B) in order to include "Replacement Sheet" in the top margin label of each sheet, in response to the outstanding objection.

In the Office Action, the Examiner rejected claims 1-5, 7-9 and 14, 15 and 17-21 under 35 U.S.C. §101 because the claimed invention is allegedly directed to non-statutory subject matter. Also, the Examiner rejected claims 1-5 and 7-9, 14-15 and 17-21 under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, rejected claims 1-5 and 7-9 under 35 U.S.C. §103(a) as allegedly being unpatentable over Silverman (PNAS; April 24, 2001; volume 98, pages 4996-5001) in view of Clarke et al. (PNAS, 1999, volume 96, pages 7232-7237), and rejected claims 14-15 and 17-21 under 35 U.S.C. §103(a) as allegedly being unpatentable over Silverman in view of Clarke et al. as applied to claims 1-5 and 7-9, in further view of Michaud (United States Patent No. 4,017,721).

The comments of the Examiner in forming the rejections are acknowledged and have been carefully considered.

Section 101 Rejection

In the Office Action, the Examiner rejected claims 1-5, 7-9 and 14, 15 and 17-21 under 35 U.S.C. §101 as allegedly being directed to non-statutory subject matter. Specifically, the Examiner stated on page 5 of the Office Action that

> the instant methods of the claims to not produce any tangible result. This aspect of the rejection may be overcome by indicating the form by which the output is given to the user....

Applicant, as proposed herein, has amended independent claims 1, 14 and 21 to include the limitation of outputting the global linear hydrophobic moment to at least one of a user, a display, a memory and one or more additional computers on a network. Support for the amendment can be found, for example, on page 11, line 5 through page 12, line 20. As such, Applicant respectfully asserts that the amendment overcomes the aspect of the rejection noted above.

The Examiner also stated on page 5 of the Office Action that

> [i]t is not comprehended as to how a "characterization" of an "amphiphilicity" is a tangible quantity, result, or "thing" that is capable of being output.

Applicant submits that the amendment highlighted above overcomes this aspect of the rejection as well. Therefore, Applicant respectfully asserts that independent claims 1, 14 and 21, as amended, overcome the §101 rejection. Also, Applicant further submits that by virtue of their dependence on allowable independent claims 1 and 14, claims 2-5, 7-9 and 15, 17-20, respectively, are directed to statutory subject matter in their own right.

Thus, Applicant respectfully requests reconsideration and withdrawal of the rejection of claims 1-5, 7-9 and 14, 15 and 17-21 under 35 U.S.C. §101.

Section 112, Second Paragraph Rejection

In the Office Action, the Examiner rejected claims 1-5, 7-9 and 14, 15 and 17-21 under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to

particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Specifically, the Examiner stated on page 6 of the Office Action that

> [i]n the final steps of claim 1, 14 and 21, there is a step of outputting a characterization. Since a characterization is not a "thing," it is unclear as to how it can be output. Consequently, the metes and bounds of "characterization" are unclear.

Applicant, as noted above, has amended independent claims 1, 14 and 21 to include the limitation of outputting the global linear hydrophobic moment to at least one of a user, a display, a memory and one or more additional computers on a network. As such, Applicant respectfully asserts that the amendment overcomes the rejection. Thus, Applicant respectfully requests reconsideration and withdrawal of the rejection of claims 1-5, 7-9 and 14, 15 and 17-21 under 35 U.S.C. §112, second paragraph.

Section 103(a) Rejection # 1

The Examiner rejected claims 1-5 and 7-9 under 35 U.S.C. §103(a) as allegedly being unpatentable over Silverman [PNAS; April 24, 2001; volume 98, pages 4996-5001] (hereinafter referred to as "Silverman") in view of Clarke et al. [PNAS, 1999, volume 96, pages 7232-7237] (hereinafter referred to as "Clarke").

On page 9 of the outstanding Office Action, the Examiner stated that

> [w]hile Silverman demonstrates his technique for a secondary structural component of a protein, Silverman does not show his method for entire proteins.
>
> Clarke et al. shows an isolated single structural element (i.e. a single alpha-helical peptide) comprising an entire protein.

Applicant respectfully submits that the amendments to independent claim 1 overcome the above-noted rejection. Specifically, Applicant notes that the Examiner, on page 8 of the Office Action, states that "In equations [13] and [14] on page 4998 of Silverman, distance metrics, ellipsoidal metrics, and a solvent accessibility are all used to enhance the centroid magnitude." Applicant respectfully asserts that the metrics taught in Silverman are only applied to second- and zero- order moments. As taught and now claimed herein, a calculation of a first order moment (the hydrophobic dipole) of an arbitrary structure is

performed, and a correlation between residue centroid magnitude and residue solvent accessibility is enhanced using a distance metric in an effort to define the global linear hydrophobic moment. Applicant respectfully asserts that a first-order moment is completely different from a zero- and/or a second-order moment.

Applicant points to page 5001, left column, of the Silverman reference, wherein it is stated that

> [t]his paper has focused on the spatial region of transition between the hydrophobic core and hydrophilic exterior of globular proteins. The moment calculations have identified two features, apparently independent of protein size and fold, that are comparable for the 30 protein structures obtained from the PBD and for the 14 native structures of the decoy set. One, a global feature, is the overall shape or profile of the second-order ellipsoidal moment calculated from protein interior to exterior. The other, a specific features, the hydrophobic ratio, is the ratio of distances at which the second- and zero-order moments of the distribution vanish. (Emphasis added).

Applicant also highlights the present specification, beginning on page 8, line 1, wherein it is stated that

> [t]he correlation between residue centroid magnitude and residue solvent accessibility is enhanced, as shown in step 106 of FIG. 1. An exemplary embodiment for enhancing the correlation between residue centroid magnitude and residue solvent accessibility is described below in conjunction with the description of FIG. 2. Thus, when defining the global linear hydrophobic moment, each residue centroid contributes a magnitude and direction to the global linear hydrophobic moment, as shown in step 108 of FIG. 1. Further... each residue centroid having the same fractional distance to the surface of the tertiary protein structure will contribute an equivalent magnitude of the global linear hydrophobic moment. An accurate determination of the magnitude of the global linear hydrophobic moment is important.... Therefore, one feature that should be modified in Equation 3 [first-order hydrophobic moment] is the lever arm dependence of each hydrophobic moment.... As can be seen in FIG. 2, a residue near the exterior of a protein and also near the major principal axis is at a greater distance from the center of the protein than a residue near the exterior of the protein but near the minor principal axis.... Even though the two residues are at the same fractional distance to the protein surface, the distance from the origin is different. The two residues would therefore make different contributions to the magnitude of the vector... in Equation 3. This difference can be corrected based on a spatial linear moment of each residue by mapping the ellipsoidal coordinates onto a sphere with radius equal to the major principal axis.... Since each residue

> then has an approximately equivalent magnitude, it may be assumed that they contribute an equal magnitude to the global linear hydrophobic moment. With this mapping, Equation 3 is written as [Equation 10]....

As a result, Applicant respectfully asserts that even if properly combined, the above-cited references do not teach or suggest all of the claimed limitations of independent claim 1. The references do not teach or suggest calculating a first-order hydrophobic moment, enhancing correlation between residue centroid magnitude and residue solvent accessibility, wherein the correlation between residue centroid magnitude and residue solvent accessibility is enhanced using a distance metric, using the first-order hydrophobic moment to define the global linear hydrophobic moment, wherein each of the residue centroids contributes a magnitude and direction to the global linear hydrophobic moment, and using the global linear hydrophobic moment to characterize an amphiphilicity of a tertiary protein structure. To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). Therefore, Applicant respectfully requests withdrawal of the §103(a) rejection.

Applicant further submits that by virtue of their dependence on allowable independent claim 1, claims 3-5 and 7-9 recite patentable subject matter in their own right. As such, Applicant respectfully requests reconsideration and withdrawal of the rejection of claims 1 2-5 and 7-9 under 35 U.S.C. 103(a).

Section 103(a) Rejection # 2

The Examiner also rejected claims 14-15 and 17-21 under 35 U.S.C. §103(a) as allegedly being unpatentable over Silverman in view of Clarke as applied to claims 1-5 and 7-9 above, in further view of Michaud [USPAT 4,017,721].

On page 14 of the outstanding Office Action, the Examiner stated that

> [i]t would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify Silverman in view of Clarke et al. as evidenced by "Glossary of Medical Terms" as evidenced by the definition of "protein tertiary structure" as applied to claims 1-5 and 7-9 above in further view of Michaud because the invention of Michaud has the advantage of using a computerized system to calculate centroids of

objects which provide a more efficient means of calculating physical aspects of objects (i.e. physical aspects of proteins) than calculation by hand.

Applicant respectfully traverses the Examiner's rejection on the grounds that the proposed combination of references is improper, and even if the combination were proper, all the limitations of the independent claims are not taught or supported by the combination. To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974).

As detailed above, Silverman in view of Clarke does not teach or suggest the claim limitation of calculating a first-order hydrophobic moment, enhancing correlation between residue centroid magnitude and residue solvent accessibility, wherein the correlation between residue centroid magnitude and residue solvent accessibility is enhanced using a distance metric, using the first-order hydrophobic moment to define the global linear hydrophobic moment, wherein each of the residue centroids contributes a magnitude and direction to the global linear hydrophobic moment, and using the global linear hydrophobic moment to characterize an amphiphilicity of a tertiary protein structure. Therefore, all of the claimed limitations of claims 14 and 21 are not taught or suggested by the prior art, and as a result, Applicant respectfully asserts that amended independent claims 14 and 21 overcome the rejection as allegedly unpatentable over the references cited in this rejection.

Furthermore, Applicant respectfully submits that Michaud uses the "centroid" of the outline of the figure for positioning, whereas the "centroid" used in the claimed invention is calculated very differently, namely from the distribution of centroids of all of the amino acid residues. As a result, these two "centroids" are very different and therefore using Michaud in combination with the above-noted references is improper.

Also, Applicant further submits that by virtue of their dependence on allowable independent claim 14, claims 15 and 17-20 recite patentable subject matter in their own right. If an independent claim is nonobvious under 35 U.S.C. 103, then any claim depending therefrom is nonobvious. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed.

Cir. 1988). Therefore, Applicant respectfully requests withdrawal of the §103(a) rejection from claims 14-15 and 17-21.

All of the pending claims, i.e., claims 1, 3-5, 7-9, 14, 15, 17 and 19-21, are in condition for allowance and such favorable action is earnestly solicited.

If any outstanding issues remain, or if the Examiner has any further suggestions for expediting allowance of this application, the Examiner is invited to contact the undersigned at the telephone number indicated below.

The Examiner's attention to this matter is appreciated.

Respectfully submitted,

Date: October 31, 2007

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Ex. A Replacement Sheets of Drawings - exemplary (7 sheets)